



An Introduction to the NIH Clinical Trials Policies

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TODAY'S FOCUS

1

PURPOSE FOR THE NEW
NIH CLINICAL TRIAL
REFORMS

2

INTRODUCTION TO THE
NIH CLINICAL TRIAL
POLICIES

3

RESOURCES TO HELP
NAVIGATE
THE NIH POLICIES
CHANGES

Why the changes?


BMJ

BMJ 2011;344:d7292 doi: 10.1136/bmj.d7292 (Published 3 January 2012)

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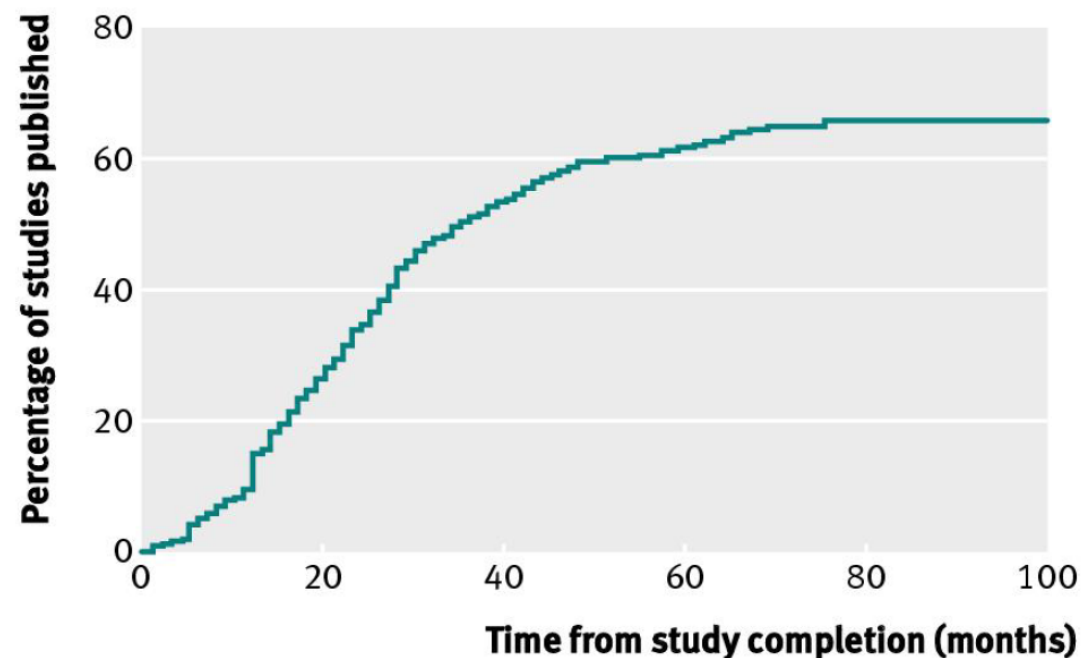
RESEARCH

Publication of NIH funded trials registered in ClinicalTrials.gov: cross sectional analysis

 OPEN ACCESS

Joseph S Ross *assistant professor of medicine*^{1,2}, Tony Tse *program analyst at ClinicalTrials.gov*³, Deborah A Zarin *director of ClinicalTrials.gov*³, Hui Xu *postgraduate house staff trainee*⁴, Lei Zhou *postgraduate house staff trainee*⁴, Harlan M Krumholz *Harold H Hines Jr professor of medicine and professor of investigative medicine and of public health*^{2,5,6}

“There are many [NIH-funded] trials not covered by [FDAAA], such as trials of behavioral interventions and surgical procedures. **No policies exist** to make sure that the public has access to results from NIH funded research that is not published”



No at risk

635 635 635 635 493 330 220 153 95 54 44

Purpose of Reforms & Policy Changes

In 2016, NIH announced initiatives targeted to enhance and improve:

Efficiency

Enhance the efficiency of how research studies involving human participants are conducted

Transparency

Promote a culture of transparency in research in order to advance public health

Accountability

Ensure that NIH can appropriately identify and report on their clinical trials portfolio to ensure proper stewardship

Timely Reporting

Decrease the time it takes investigators to publicly report study results

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TOP 10 NIH POLICY CHANGES TO ENHANCE STEWARDSHIP



POLICIES RELEVANT TO *ALL* RESEARCH INVOLVING HUMAN PARTICIPANTS

Single IRB
January 25,
2018

New
Application
Forms
January 25,
2018

- ✓ Use of a single Institutional Review Board (IRB) for multi-site studies
- ✓ New forms to collect human subjects information
- ✓ Certificates of confidentiality for all research that uses identifiable, sensitive information
- ✓ Expands the Inclusion of Children as Participants in Clinical Research Policy to include individuals of all ages, including older adults

Certificate of
Confidentiality
January 25,
2018

Inclusion
across the
Life Span
January 25,
2019

Single IRB
January 25,
2018

SINGLE INSTITUTIONAL REVIEW BOARD (sIRB)

NOT-OD-16-094: All domestic multi-site studies will use sIRB for ethical review required of non-exempt humans subjects research protocols

Must include a plan that describes:

- The use of a sIRB selected to serve as the IRB of record
- How communications between sites and sIRB will be handled

Standardized agreements have been developed that allow institutions to rely on a sIRB

Exceptions: sIRB not applicable for Career Development (K), Research Training (T), or Fellowship (F) grants

TIP: NCATS SMART IRB platform is a resource for investigators
(SMART: Streamlined, Multisite, Accelerated Resources for Trials)

New
Application
Forms
NOW!

CHANGES TO THE APPLICATION PACKAGE

(NOT-OD-17-062: FORMS-E Application Guide & Package)

PHS Human Subjects and Clinical Trials Information Form

The image shows a stack of three overlapping screenshots of the PHS Human Subjects and Clinical Trials Information Form. The top screenshot is the 'Delayed Onset Study' form, which includes a 'Study Title' field and a 'Required field(s)' section. The middle screenshot is the 'Inclusion Enrollment Report' form, which includes a 'Study Title' field and a 'Required field(s)' section. The bottom screenshot is the 'Section 4 - Protocol Synopsis' form, which includes a 'Brief Summary' field, a 'Study Design' field, and a 'Narrative Study Description' field.

- Collects human subjects, inclusion enrollment, and clinical trial information at the study-level
- Protocol Synopsis, Statistical Plan,
- Includes a Clinical Trials Questionnaire

TIP: Watch the NIH Video that walks through the PHS Human Subjects and Clinical Trials Information Form

ADDITIONAL NIH POLICIES FOR CLINICAL TRIALS

Clinical
Trial FOAs
January 25,
2018

- ✓ Clinical trial-specific Funding Opportunity Announcements (FOAs)
- ✓ New review criteria
- ✓ Expanded registration and results reporting in ClinicalTrials.gov
- ✓ Training in Good Clinical Practice (GCP)

Trial Review
Criteria
January 25,
2018

Registration
& Reporting
Effective Now!

Good
Clinical
Practice
Effective
Now!

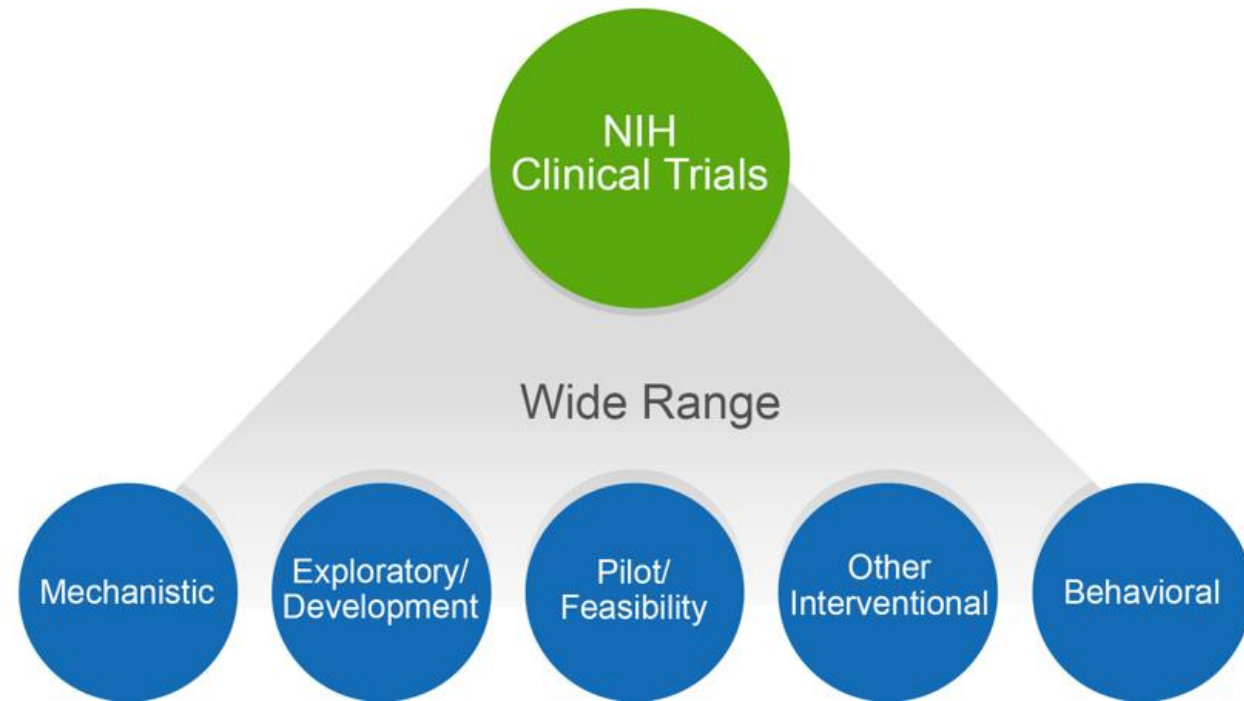
How Does NIH Define a Clinical Trial?

A research study in which one or more **human subjects** are **prospectively assigned** to one or more **interventions** (which may include placebo or other control) to evaluate the effects of those interventions on **health-related biomedical or behavioral outcomes**.

Learn more at <https://grants.nih.gov/policy/clinical-trials/definition.htm>

NIH Definition of a Clinical Trial is Broad

- Definition was **clarified** and **broadened** in October 2014
- Encompasses a wide range of types of trials, including:
 - Mechanistic
 - Exploratory
 - Pilot/Feasibility
 - Behavioral
- With broader definition, many more studies are classified as clinical trials



CLINICAL TRIAL QUESTIONNAIRE

Does the study...

1. Involve one or more human subjects?
2. Prospectively assign human subject(s) to one or more intervention(s)?
3. Evaluate the effect of intervention(s) on the human subject(s)?
4. Have a health-related biomedical or behavioral outcome?

If “yes” to ALL – it’s a clinical trial

THIS WILL REQUIRE:

- Appropriate FOA Selection
- Writing of research strategy & human subjects sections
- Addressing additional review criteria for clinical trials
- Registering & reporting the trial in ClinicalTrials.gov

Unsure how to answer the questions? We have a tool that can help! <https://grants.nih.gov/ct-decision/>

Clinical
Trial FOAs
January 25,
2018

CLINICAL TRIAL-SPECIFIC FUNDING OPPORTUNITY ANNOUNCEMENTS

NOT-OD-16-147: All clinical trial applications **MUST** be submitted to an FOA that allows clinical trials

- Clinical Trial - Not Allowed
- Clinical Trial - Optional
- Clinical Trial – Required
- Basic Experimental Studies with Humans (BESH) Required
- Special circumstances for career development awardees –
see <https://grants.nih.gov/policy/clinical-trials/specific-funding-opportunities.htm>

How to Determine if an FOA Accepts Clinical Trials?

FOA Title (new FOAs only)

FOA Section II. Award Information

Participating Organization(s)

National Institutes of Health ([NIH](#))

Components of Participating Organizations

National Cancer Institute ([NCI](#))

Funding Opportunity Title

Early Phase Clinical Trials in Imaging and Image-Guided Interventions (R01 Clinical Trial Required)

Application Types Allowed

New

Resubmission

Revision

The [OER Glossary](#) and the SF424 (R&R) Application Guide provide details on application types.

Clinical Trial?

Required: Only accepting applications that propose clinical trial(s)

[Need help determining whether you are doing a clinical trial?](#)

Tip: Check your FOA at least 30 days before the due date for any updates



NEW NCI CLINICAL TRIAL FUNDING OPPORTUNITIES

NCI DOES NOT PARTICIPATE IN NIH CLINICAL
TRIAL-REQUIRED PARENT R01 & R21

PAR-18-560

DCTD Parent R01- Clinical Trial Required

Investigator-initiated Early Phase Clinical Trials for Cancer Treatment and Diagnosis

PAR-18-559

DCP-DCCPS Parent R01-Clinical Trial Required

Cancer Prevention and Control Clinical Trials Grant Program

<https://www.cancer.gov/grants-training/grants-funding/funding-opportunities>

Basic Experimental Studies with Humans (BESH)

Who: Investigators for studies whose primary purpose is the pursuit of basic science and that meet the NIH definition of a “clinical trial” and also the Federal definition of basic science

What: *Delayed Enforcement and Short-Term Flexibilities for Some Requirements Affecting Prospective Basic Science Studies Involving Humans (NOT-OD-18-212)* -- must register and report but can do so through existing basic science portals

When: *Release Date:* July 20, 2018
Effective Through: September 24, 2019

For more information see: <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-212.html>

REVIEW CRITERIA FOR CLINICAL TRIALS

NOT-OD-17-118: FOAs that accept clinical trials will
include new review criteria

Scored Review Criteria

- ✓ Significance
- ✓ Investigator
- ✓ Innovation
- ✓ Approach
- ✓ Environment

Additional Review Criteria

- ✓ Study Timeline & Milestones

Read the FOA carefully and
be sure your application
addresses the review
criteria appropriately

Registration
& Reporting
Effective Now!

DISSEMINATION OF NIH-FUNDED CLINICAL TRIAL INFORMATION NOT-OD-16-149

Who: All investigators conducting clinical trials funded in whole or in part by the NIH regardless of trial phase

What: Sponsors need to register* and report results** of trials in ClinicalTrials.gov

Why: Increase the availability of information about clinical trials and their results to the public in a timely manner

*within 21 days of 1st patient enrollment

**no later than 1 year after trial's primary completion date



GOOD CLINICAL PRACTICE TRAINING REQUIREMENT

- Who:** All NIH-funded investigators and NCI staff involved in the *conduct, oversight or management* of clinical trials
- What:** Both are expected to be trained in GCP consistent with principles of the International Council on Harmonisation
- Why:** To assure the safety, integrity, and quality of clinical trials
- How:** Through a class or course, academic training program, or certification from a recognized clinical research professional organization

NOTE: CERTIFICATES SHOULD BE MADE
AVAILABLE TO NIH UPON REQUEST



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VISIT THE NIH OFFICE OF EXTRAMURAL RESEARCH FOR DETAILS

<https://grants.nih.gov/policy/clinical-trials.htm>

The screenshot shows the NIH Grants & Funding website. The header includes the NIH logo, "National Institutes of Health Office of Extramural Research", and "Grants & Funding NIH's Central Resource for Grants and Funding Information". A navigation bar has links for HOME, ABOUT GRANTS, FUNDING, POLICY & COMPLIANCE (highlighted), and NEWS & EVENTS. A breadcrumb trail reads: Home » Policy & Compliance » Clinical Trial Requirements for Grants and Contracts. The left sidebar lists "Policy & Compliance" with sub-links: NIH Grants Policy Statement, Notices of Policy Changes, Compliance & Oversight, Select Policy Topics (Animal Welfare, Application Submission Policies), Clinical Trial Requirements (highlighted), Clinical Trial Definition, Why the Changes, Good Clinical Practice, Specific Funding Opportunities, Clinical Trial-Specific Review Criteria, New Form, and Single IRB Policy. The main content area is titled "Clinical Trial Requirements for Grants and Contracts" and states: "NIH is launching a series of initiatives that are rolling out in 2017-2018 to enhance the accountability and transparency of clinical research. These initiatives target key points along the whole clinical trial lifecycle from concept to results reporting. Learn more about these changes and how they will affect your research." Below this is the "NIH Definition of a Clinical Trial": "A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes. Learn more". A callout box says: "Your human subjects study may meet the NIH definition of a clinical trial. FIND OUT HERE". A diagram shows a green circle at the top labeled "NIH Clinical Trials" connected by lines to a row of five blue circles below, labeled "Mechanistic", "Exploratory/Development", "Pilot/Feasibility", "Other Interventional", and "Behavioral". The text "Wide Range" is centered above the bottom row of circles.

Training Resources:

<https://grants.nih.gov/policy/clinical-trials/training-resources.htm>

- ✓ Slides
- ✓ Human Subjects/Clinical Trials Questionnaire
- ✓ Videos
- ✓ Training opportunities



**NATIONAL
CANCER
INSTITUTE**

www.cancer.gov

www.cancer.gov/espanol